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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,442	02/10/2004	Moses Rodriguez	2609/60726-AZ/JPW/GJG/DJK	3701

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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,442	RODRIGUEZ ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b)

Status

1)☒ Responsive to communication(s) filed on *25 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,30-34,36,37,41,42 and 54-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30-34,36,37,41,42 and 54-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

Applicant's amendment filed August 25, 2006 is acknowledged. Claims 1-27, 29, 35, 8-40 and 43-53 are cancelled. Claims 28, 30-34, 36, 37, 41, 42, and newly added claims 54-60 are pending in this application and under examination in light of treating a subject suffering from multiple sclerosis comprising administering humanized antibody against an epitope on glatiramer acetate. The text of those sections of Title 35, U.S. Code, not included in this action can be found in the prior office action.

Claim Rejections/Objections Withdrawn

The objection to claims 35 and 38 is withdrawn in response to Applicant's cancellation of the claims.

The rejection of claim 31 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendment to the claim.

The rejection of claims 34 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendment to claim 34 and cancellation of claim 35.

The rejection of claims 29 and 38 under 35 U.S.C. 112, first paragraph, because the specification is not enabling the invention commensurate in scope with the claims is moot because the claims are canceled.

The rejection of Claims 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over either of Rodriguez et al. (U.S. Patent 5591629 issued on Jan 7, 1997 as in IDS submitted Feb 10,2004) or Warrington et al. (Proc. Natl. Acad. Sci. USA. June 6, 2000. 97:6820-6825) in view of Arnon et al. (U.S. Patent No. 6214791 issued on Apr 10, 2001 as in IDS submitted Dec 03, 2004) and Teitelbaum et al. (Pro. Natl. Acad. Sci. USA 1991, 88: 9528-9532) is moot because the claims are canceled.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 112

The rejection of Claims 28, 30-34, 36, 37, 41, 42 under 35 U.S.C. 112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is maintained for reasons of record in the previous office action. The rejection is also applied to the newly added claims 54-60 because the new claims 54-60 recite the same limitation as in original claims.

Applicant argues that the amended claims meet the requirement of enablement because they recite multiple sclerosis and a humanized antibody. Applicant argues that the TMEV animal model provides a reasonable correlation with multiple sclerosis as in the claimed invention because the TMEV animal model is one of the best models for multiple sclerosis and further cites Oleszak et al. (Clin. Microbiol. Rev. 2004. 17: 174-207) to support the argument. Applicant argues that a better correlation would be clinical tests in human and the clinical trial in the human requires a FDA approval, which is not prerequisite for finding if a compound is useful. Applicant argues that there is no

undue experimentation required for a skilled artisan to practice the claimed invention because the specification provides sufficient guidance that includes a correlation of the TMEV animal model with multiple sclerosis and administering to the animal with a humanized antibody against an epitope on glatiramer acetate to treat multiple sclerosis.

Applicant's arguments have been fully considered but they are not found persuasive. In response to Applicant's argument about clinical tests in human, Applicant is not required to provide clinical tests in human to show the usefulness of a test compound. In response to Applicant's argument that the TMEV model is one of the best models for MS and provides a reasonable correlation with MS, it is noted that although the TMEV animal model shows some pathological features similar to MS, the cause of TMEV animal model is mainly due to the viral infection, which is different from MS. The pathogenesis of MS has been suggested due to a TH-1 type cell mediated immune response to myelin sheath resulting in inflammation and degeneration in the nervous system (t'Hart et al. Curr. Opin. Neurol. 2003. 16: 375-383 cited in the previous office action). Although the reference of Oleszak et al. submitted by Applicant describes some similarity of pathological phenotypes between the TEMV animal and MS, t'Hart et al. teach that the TMEV model only reflects partial pathological features of MS (t'Hart et al. Curr. Opin. Neurol. 2003. 16: 375-383 cited in the previous office action). In addition, the pathogenesis of MS is very heterogeneous (t'Hart et al. Curr. Opin. Neurol. 2003. 16: 375-383 cited in the previous office action), indicating that the effects of anti-glatiramer acetate antibody on the TEMV animal model do not necessarily occur in MS patients since the cause of MS is much more complex. Further, Franklin teaches that

although several agents have been shown to enhance remyelination in experimental animal models, none of them has become a routine clinical therapy for MS because the basis of the effects remains obscure and the possible reason is due to failure of remyelination in MS patients (p. 705, 2nd col, 2nd paragraph, Franklin. Nat. Rev. Neurosci. 2002. 3: 705-714). Remyelination failure has been suggested due to recruitment failure of oligodendrocyte precursor cells (OPC), failure of OPC differentiation and adverse signal environment created by demyelination, which is not good for remyelination (p. 705, 2nd col, 2nd paragraph). Franklin also teaches that in experimental models, repeated rounds of demyelination and remyelination lead to less efficient remyelination, which occurs in MS (p. 707, 2nd col. remyelination failure). Moreover, several agents that show promising in animal models of MS fail in MS patients and the main reasons for failure were due to lack of efficacy and/or unexpected adverse effects. For example, an anti-α4-integrin antibody, which has been shown promising results in the EAE animal model (another mouse model of MS) and approved for clinical trials by FDA, causes progressive multifocal leukoencephalopathy (PML, an oligodendroglial viral disease associated with decreased cellular immunity) in MS patients (Fontoura et al. Int. Rev. Immunol. 2005. 24: 415-6). The above finding suggests that the positive results demonstrated in an animal model do not reflect the true effects in patients. The instant claims are not limited to an animal model of MS. However, Applicant fails to provide sufficient guidance as to whether the effects of anti-glatiramer acetate in remyelination in TEMV animal would obtain in patients suffering from MS, which has a more heterogeneous and complex pathogenesis. Thus, it is

unpredictable to treat MS patients by using a humanized anti-glatiramer acetate sine neither the specification nor the prior art teaches that anti-glatiramer acetate antibody is able to effectively treat MS and also has no adverse effects on patients.

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more
predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004)" See MPEP § 2164.03

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular,
the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03

The specification has not provided sufficient guidance as to enable one skill in the art to practice the claimed invention without undue experimentation commensurate in scope with these claims. Therefore, in view of the breath of claims, the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention. Accordingly, the rejection of claims 28, 30-34, 36, 37, 41, 42, 54-60 under 35 U.S.C. 112, first

paragraph, because the specification is not enabling the invention commensurate in scope with the claims is maintained.

Claim Rejections - 35 USC § 103

The rejection of Claims 28, 30-34, 36, 37, 41 and 42 under 35 U.S.C. 103(a) as being unpatentable over either of Rodriguez et al. (U.S. Patent 5, 591, 629 issued on Jan 7, 1997 as in IDS submitted Feb 10,2004) or Warrington et al. (Proc. Natl. Acad. Sci. USA. June 6, 2000. 97:6820-6825) in view of Arnon et al. (U.S. Patent No. 6214791 issued on Apr 10, 2001 as in IDS submitted Dec 03, 2004) and Teitelbaum et al. (Pro. Natl. Acad. Sci. USA 1991, 88: 9528-9532) is maintained for reasons of record in the previous office action. The rejection is also applied to newly added claims 54-60 since new claims 54-60 also recite the limitation as in original claims.

Applicant argues that amended claims include the subject matter that is not subject to the rejection because claim 29 was not rejected under *35 USC § 103*. Applicant's arguments have been fully considered but they are not persuasive because U.S. Patent 5,591,629 also teaches a humanized antibody of SCH94.03 (see col 13, line 44-50). '629 teach that an IgM monoclonal antibody SCH94.03 is able to promote CNS remyelination in one of the MS mouse models induced by infection of TEMV. Warrington et al. teach that human polyclonal and monoclonal IgM and IgG are able to promote oligodendrocyte remyelination in the MS mouse model induced by infection of TEMV. The teachings of '629 and Warrington et al. meet the limitation of administering to a subject with humanized anti-glatiramer acetate antibody as in claims 28, 30-34, 36,

37, 41, 42, 50-60 (see col. 5-7). U.S. Patent No. 6214791 teaches using Copolymer 1/glatiramer acetate as a therapeutic agent through ingestion or inhalation to treat multiple sclerosis (see column7 Example 3). Teitelbaum et al. teach that most monoclonal anti-glatiramer antibodies do not cross-react with myelin basic protein and only some monoclonal anti-glatiramer acetate antibodies cross react with MBP (see p. 9531, first column, second paragraph) whereas one third of anti-MBP antibodies are cross reactive with glatiramer acetate. The teachings of US 6214791 and Teitelbaum et al. meet the limitation that the anti-glatiramer acetate antibody does not cross-react with MBP and cross-react with spinal cord homogenate. It would have been obvious for one of ordinary skill in the art at the time the instant invention was made to be motivated to combine the teachings of either of U.S. Patent 5,591,629, or Warrington et al., U.S. Patent No. 6214791, with Teitelbaum et al. to administer a humanized antibody against an epitope on glatiramer acetate in promoting remyelination in the MS mouse model induced by TEMV since glatiramer acetate has been shown to activate T cell activity and subsequently protect nerve cells from toxicity. In addition, the anti-glatiramer acetate antibody has been shown to either cross react or not cross react with MBP and the antibody SCH94.03 against spinal cord homogenates has been shown to promote remyelination in MS mouse animal model induced by TEMV. Thus, one of ordinary skill in the art would have expected success in promoting oligodendrocyte remyelination in the TEMV animal model of MS by administering an anti-glatiramer acetate antibody, which is not cross reactive with MBP or oligodendrocytes, in the test animals. Thus, the rejection of Claims 28, 30-34, 36, 37, 41, 42, 50-60 under 35 U.S.C. 103(a) as being

unpatentable over either of Rodriguez et al. (U.S. Patent 5, 591, 629 issued on Jan 7, 1997 as in IDS submitted Feb 10,2004) or Warrington et al. (Proc. Natl. Acad. Sci. USA. June 6, 2000. 97:6820-6825) in view of Arnon et al. (U.S. Patent No. 6214791 issued on Apr 10, 2001 as in IDS submitted Dec 03, 2004) and Teitelbaum et al. (Pro. Natl. Acad. Sci. USA 1991, 88: 9528-9532) is maintained.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
October 23, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER